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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/071,751	02/07/2002	Shirley Wu Hunter	2618-17-C4-PUS-2	2578

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EXAMINER	
STEADMAN, DAVID J	
ART UNIT	**PAPER NUMBER**
1656	

DATE MAILED: 12/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/071,751	HUNTER ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *69-75 and 77-81* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *69-71* is/are allowed.

6)☒ Claim(s) *72-75 and 77-81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1656.

[2] Claims 69-75 and 77-81 are pending in the application.

[3] Applicants' amendment to the claims, filed on 10/12/2005, is acknowledged and has been entered into the application. This listing of the claims replaces all prior versions and listings of the claims.

[4] Receipt of a sequence listing in computer readable form (CRF), a paper copy thereof, a statement of their sameness, a statement that no new matter has been added to the specification by the paper copy of the sequence CRF, and an amendment to the specification directing entry of the sequence listing, all filed on 10/12/2005, is acknowledged.

[5] Applicant's arguments filed on 10/12/2005 in response to the Office action mailed on 6/8/2005 have been fully considered and are deemed to be persuasive to overcome some of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[6] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Claim for Domestic Priority

[7] Applicant claims domestic priority to US non-provisional application 09/171,156 and international application PCT/US97/05959. As previously noted, while the sequences of SEQ ID NO:61 and 62 of the sequence listing filed on 2/7/2002 are supported by the disclosure of application 09/171,156, the sequences of SEQ ID NO:61 and 62 filed on 2/7/2002 are *not* supported by the disclosure of application PCT/US97/05959 as SEQ ID NO:61 and 62 of application PCT/US97/05959 (pp. 146-147 of WO 97/37676) are not identical to SEQ ID NO:61 and 62, respectively, of the instant application. See Appendices A and B of the Office action mailed on 6/8/2005. In the instant response, applicant asserts that SEQ ID NO:61 and 62 of the sequence listing filed on 2/7/2002 are identical to the corresponding sequences in the sequence listing filed in application PCT/US97/05959. However, this is not the case. A review of the sequence listing filed on 2/7/2002 reveals that AAT is present at nucleotide positions 328-330 of SEQ ID NO:1 (shown as encoding an isoleucine) and isoleucine is present at amino acid position 110 of SEQ ID NO:62. Neither of these sequences was present in the *originally filed* application 09/171,156. However, it is noted that applicant has properly incorporated the priority documents by reference in a specification amendment in the transmittal letter filed on 2/7/2002. Thus, amending the sequence of SEQ ID NO:61 and 62 such that they are identical to SEQ ID NO:61 and 62, respectively, of PCT/US97/05959 (*i.e.,* replacing A with T at nucleotide 329 of SEQ ID NO:61 and replace Ile with Asn at position 110 of SEQ ID NO:62) is not considered to be new matter. Because the sequences of SEQ ID NO:61 and 62 of the sequence listing filed

on 10/12/2005 are supported by both the '156 application and PCT/US97/05959, the disclosures of which are properly incorporated by reference herein, applicant is granted the benefit of priority to the filing date of PCT/US97/05959, *i.e.,* 4/10/1997.

Claim Objection(s)

[8] Claims 74-75 are objected to in the recitation of "wherein said 6 amino acid sequence." Claims 74-75 depend from claim 72, which is drawn to (in relevant part) "[a] fragment of at least 6 contiguous amino acids." In order to maintain consistency in the claims, it is suggested that the phrase "wherein said 6 amino acid sequence" in claims 74-75 be replaced with, for example, "wherein said at least 6 contiguous amino acid sequence."

Claim Rejections - 35 USC § 112, Second Paragraph

[9] Claims 77-81 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is necessitated by amendment.

Claim 77 (claim(s) 78-81 dependent therefrom) is indefinite in the recitation of "the nucleotide sequence amplified from flea salivary gland DNA by the polymerase chain reaction..." as it is unclear as to *the* nucleotide sequence that is referenced in the claim. It is well-known in the prior art that a nucleic acid that is amplified by PCR under certain conditions will not necessarily be amplified under other PCR conditions. Alternatively, under certain conditions, a plurality of nucleic acids are amplified due to

non-specific annealing of primers to a nucleic acid template. See Rychlik et al. (*Nuc Acids Res* 18:6409-6412), which teaches that under sub-optimal annealing temperatures, "non-specific products were formed" during a PCR amplification reaction. Consequently, it is unclear as to the scope of claimed proteins, which are encoded by the amplified nucleic acid. It is suggested that applicant clarify *the* nucleic acid that is intended as being amplified from flea salivary gland DNA.

Claim Rejections - 35 USC § 101

[10] Claims 72-75 and 79-81 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are drawn to a protein fragment. Such fragments occur in nature as a result of, *e.g.,* post-translational processing events. The claims read on a product of nature and should be amended to indicate the hand of the inventor, e.g., by insertion of "purified" or "isolated". See MPEP § 2105.

Claim Rejections - 35 USC § 112, First Paragraph

[11] Claims 77-81 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of he claimed invention. This is a new matter rejection and is necessitated by amendment.

MPEP § 2163 states, "when filing an amendment an applicant should show support in the original disclosure for new or amended claims" and "[i]f the originally filed disclosure does not provide support for each claim limitation, or if an element which applicant describes as essential or critical is not claimed, a new or amended claim must be rejected under 35 U.S.C. 112, para. 1, as lacking adequate written description".

Claim 77 (claim(s) 78-81 dependent therefrom) is drawn to a protein that is encoded by any nucleic acid that is amplified from flea salivary gland DNA by the polymerase chain reaction using SEQ ID NO:81/82 as a primer pair for amplification. As support for the recited limitation, applicant points to pp. 29 and 94-95 of the specification (see p. 8, top, of the instant response). However, the cited disclosure does not support the claim limitations. The disclosure at p. 29 is not related to PCR and is instead related to cell transformation or transfection. Pages 94-95 of the specification disclose PCR amplification under an undisclosed set of PCR conditions to produce a *specific* nucleic acid, namely, $nfspl_{474}$, using a *specific* template, *i.e.,* , $nfspl_{1007}$. The disclosure does not teach amplification of flea salivary gland DNA to produce any nucleic acid that is amplified by SEQ ID NO:81/82 under any PCR conditions. Consequently, applicant's cited disclosure fails to "show support" for the claimed protein. It is suggested that applicants show support for the recited limitation.

[12] Claims 77-81 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of he claimed invention. This rejection is necessitated by amendment.

Claims 77-81 are drawn to a genus of proteins and protein fragments that are encoded by a nucleic acid that is PCR amplified from flea salivary gland DNA using SEQ ID NO:81/82 as primers.

The Court of Appeals for the Federal Circuit has held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

In this case, the specification discloses only a single species of the genus of claimed proteins, *i.e.*, $Pfspl_{158}$, which is encoded by a nucleic acid obtained by PCR

amplification using SEQ ID NO:81/82, *i.e.*, $nfspl_{474}$ (specification at pp. 94-95). Other than this single disclosed species, the specification fails to disclose any other additional species of the genus of claimed proteins. In this case, the genus encompasses species that are widely variant in structure and function. It is well-known in the prior art that a plurality of nucleic acids are amplified from a template due to non-specific annealing of primers. See, *e.g.,* Rychlik et al. (*Nuc Acids Res* 18:6409-6412), which teaches that under sub-optimal annealing temperatures, "non-specific products were formed" during a PCR amplification reaction. Also, it is well-known in the prior art that mutations can be introduced into PCR-amplified DNA. See, *e.g.,* Keohavong et al. (*PNAS* 86:9253-9257). As such, the disclosed species of $Pfspl_{158}$ fails to represent the variation within the genus of claimed proteins.

Thus, given the lack of description of a representative number of genes, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[13] Claims 77-81 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO:62, does not reasonably provide enablement for all proteins encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. This rejection is necessitated by amendment.

It is the examiner's position that undue experimentation is required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). MPEP 2164.04 states, "[w]hile the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection" and that "[t]he language should focus on those factors, reasons, and evidence that lead the examiner to conclude that the specification fails to teach how to make and use the claimed invention without undue experimentation, or that the scope of any enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the claims." Accordingly, the Factors most relevant to the instant rejection are addressed in detail below.

The breadth of the claims: Claims 77-81 are so broad as to encompass all proteins that are encoded by nucleic acids amplified by PCR using primers SEQ ID NO:81/82 and any flea salivary gland DNA as a template. The encoded protein of claims 77-79 can have any structure and any function. The enablement provided by the specification is not commensurate in scope with the claims with regard to the broad scope of proteins

broadly encompassed by the claims. In this case, the specification is enabling only for SEQ ID NO:62.

The state of the prior art; The level of one of ordinary skill; and The level of predictability in the art: Methods of PCR amplification of a DNA using a specified set of primers was well-known in the art at the time of the invention. However, as noted above, a primer pair can non-specifically amplify nucleic acids other than the intended target as evidenced by Rychlik et al. (*supra*). Also, it is highly unpredictable as to whether the resulting amplified nucleic acid would encode a protein that would maintain the ability to elicit an immune response to SEQ ID NO:62, particularly as random mutations can be introduced into PCR-amplified DNA as evidenced by Keohavong et al. (*supra*). Also, while methods of making random variants of a nucleic acid were known in the art at the time of the invention, it was highly unpredictable as to whether such alterations would or would not disrupt the ability of an encoded protein to elicit an antibody that binds to SEQ ID NO:62. See particularly the references of Colman and Abaza et al. (cited in the Office action mailed on 5/14/2004).

The amount of direction provided by the inventor and The existence of working examples: The specification discloses a single working example of the claimed polypeptide, *i.e.,* SEQ ID NO:62. Other than this single working example, the specification fails to disclose any specific guidance for randomly or site- or region-specifically altering SEQ ID NO:62 with an expectation of obtaining a protein that elicits antibodies that bind to SEQ ID NO:62. Further, regarding claims 77-79, it is noted that

the specification fails to provide guidance for using those proteins that do not elicit antibodies to SEQ ID NO:62.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: While methods of PCR amplification were known in the art at the time of the invention, it was not routine in the art to specifically or non-specifically amplify all flea salivary gland DNAs as encompassed by the claims and screen for those that encode polypeptides having the desired activity/utility. Also, while methods of modifying or altering the sequence of a protein were known at the time of the invention, it was not routine to modify a protein and screen those having a substantial number of modifications as encompassed by the claims for those that have the desired activity/utility.

In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability as evidenced by the prior art, and the amount of experimentation required, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention. Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is

unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

[14] The rejection of claims 69-70 and 72-75 under 35 U.S.C. 102(a) as being anticipated by Frank et al. and the rejection of claim(s) 72-75 under 35 U.S.C. 102(a) as being anticipated by Database GenBank Accession Number U63555 (GI:3805686) are withdrawn in view of applicant's submission of a new sequence listing that is supported by 09/171,156 and PCT/US97/05959 such that the instant application is granted the benefit of priority of the filing date of the PCT/US97/05959 application, which is 4/10/1997. Frank et al. and GenBank Accession Number U63555, both having earliest public availability dates of 1998, are not available as prior art under 35 U.S.C. 102.

Conclusion

[15] Status of the claims:

Claims 69-75 and 77-81 are pending.

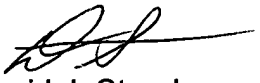
Claims 69-71 appear to be in a condition for allowance.

Claims 72-75 and 77-81 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Thurs, 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



David J. Steadman, Ph.D.
Primary Examiner
Art Unit 1656